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| EXAMINER | |
|---|---|
| EWOLDT, GERALD R | |

| ART UNIT | PAPER NUMBER |
|---|---|
| 1644 | |

DATE MAILED: 09/08/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

| Office Action Summary | Application No. | Applicant(s) | |
|---|---|---|---|
| | 10/072,425 | MOSER ET AL. | |
| | Examiner | Art Unit | |
| | G. R. Ewoldt, Ph.D. | 1644 | |

*-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --*

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

1)☒ Responsive to communication(s) filed on *25 May 2005 and 13 June 2002*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

4)☒ Claim(s) *1-3,5-14,16-24,26-35 and 37-57* is/are pending in the application.

4a) Of the above claim(s) *3,8,19,29 and 40* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,2,5-7,9-14,16-18,20-24,26-28,30-35,37-39 and 41-57* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

**Application Papers**

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

**DETAILED ACTION**

1. Claims 3, 8, 19, 29, and 40 stand withdrawn from further consideration by the examiner, 37 CFR 1.142(b), as being drawn to non-elected inventions.

Claims 4, 15, 25, and 36 have been canceled.

Claims 1, 2, 5-7, 9-14, 16-18, 20-24, 26-28, 30-35, 37-39, and 41-57 read on the elected invention and are being acted upon.

2. Applicant's amendment and remarks, filed 6/12/05, are acknowledged. In view of the amendment (correcting a typographical error), the previous rejection of Claims 47-49 under the second paragraph of 35 U.S.C. 112 has been withdrawn.

3. The new oath of Inventor Lespagnard is acknowledged.

4. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

5. Claims 1, 5, 6, 7, 9, 10, 11, 16, 17, 18, 20, 21, 22, 26, 27, 28, and 29 stand rejected under 35 U.S.C. 103(a) as being unpatentable over Guo et al. (1994, IDS) in view of Sornasse et al. (1992).

As set forth previously, Guo et al. teaches a method for producing a plurality of hybrids/hybridomas comprising a bone marrow derived antigen-presenting B cell and a tumor cell (see particularly page 520, columns 2-3, 11.). The method comprises the providing of a tumor sample and an isolated autologous B cell, and the fusing of the cells with PEG to produce a plurality of hybrids/hybridomas (see particularly page 518, column 2). The reference teaches that the hybrids/hybridomas comprise cells that express both tumor-specific antigens and the machinery for antigen presentation, i.e., characteristics of both tumor cells and B cells (see particularly page 518, column 1), that said hybrids/hybridomas are useful for the induction of an anti-tumor response in that they reduce the number of tumor cells upon administration to a subject (see particularly page 518, column 3). The reference further teaches that the hybrids/hybridomas were selected on the basis of a tumor cell surface marker and a B cell surface marker (see particularly page 518, column 3).

The reference teaching differs from the claimed invention only in that it does not teach the use of a DC as the antigen presenting component of the hybrid.

Sornasse et al. teaches that, while both B cells and DCs are capable of inducing IL2 secretion *in vitro*, DCs induce a more vigorous response, including a Th1 response, *in vivo* (see particularly pages 16-17, Results). The reference teaches the superiority of DCs over B cells for *in vivo* use, "Our data emphasize the main role of DC in initiating primary responses in vivo" (see page 18, column 1). Note that the DCs of the reference comprise splenic DCs which would include bone marrow derived DCs, lymphoid DCs, and myeloid DCs.

It would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to produce the hybrids/hybridomas of Guo et al., by the method of Guo et al., substituting a DC for the B cell in said hybrids/hybridomas, as taught by Sornasse et al. One of ordinary skill in the art at the time of the invention would have been motivated to make said substitution because, while both B cells and DCs are capable of inducing IL2 secretion *in vitro*, DCs induce a more vigorous response, including a Th1 response, *in vivo*, as taught by Sornasse et al. "Our data emphasize the main role of DC in initiating primary responses in vivo". Note that the additional limitations such as preparing a primary cell culture of the tumor cells comprises only an obvious and necessary step when said culture is not readily available as it was for Guo et al. Note, however, the BERH-2 tumor cells of Guo et al. derive from a hepatocarcinoma thus, said cells were previously the "primary culture" of tumor cells as set forth in the claims.

Applicant's arguments, filed 6/13/05, have been fully considered but they are not persuasive. Applicant argues that in the first declaration of Inventor Moser, submitted in related application 09/951,848 and 09/802,397, the Inventor argued the unpredictability of a DC/tumor hybridoma.

The Examiner's response to the Inventor's first declaration submitted in 09/802,397 (from the Office action of 6/04/04) is reiterated here.

"The Declarant argues "In my opinion, based on said documents it is not predictable that such hybrids could be made and which characteristic said hybrids would carry. Furthermore, I am convinced that the approach of Guo for making his hybrids may not be followed to produce hybrids which may be used for human applications. As the method of making said hybrids (and thus also the starting cells) are different it is clear that the resulting hybrids will be different". The Declarant continues, "Changing the fusion partner of the tumor cell, as with the B cell of Guo et al. (1994), to another antigen-presenting cell does not allow one of skill in the art to predict the outcome of such an experiment." The declarant cites Carbonne et al. (1988) in support of the arguments. The Declarant continues with numerous reasons for the asserted unpredictability."

"It is the examiner's position that the Inventor's arguments are not convincing for the following reasons. First, the teachings of Guo et al. must be considered in the context of what one of skill in the art would have known at the time of the invention. Thus, the precise methods of Guo et al. would not need to followed, some variation and routine experimentation would be allowable and still be considered obvious. Additionally, since one of ordinary skill in the art at the time of the invention would have known that DC hybridomas retaining T cell activation capability were produced as early as 1981, (see, for example, the work of J.H. Peters) the Declarant cannot convincingly argue that said hybridomas/ hybrids could not be predictably made over a decade later. Regarding the Carbonne et al. reference, a review of said reference shows that the teachings of the reference are not applicable to the instant situation. In that work the authors fused two closely related cells, one which expressed Lyt-2 (CD8) and one which did not. The point of the work was the study of Lyt-2 expression, in particular whether said expression was under positive or negative regulation during T cell development. The authors discovered trans-acting negative regulatory factors specifically provided by the cell that did not express Lyt-2 which shut down expression of the gene in the hybrid. This highly specific situation cannot be generically applied to assert unpredictability in the hybrids employed in the method of the instant claims."

"The Declarant makes a number of assertions that comprise either unclaimed limitations or irrelevant observations. The Declarant describes "major advantages" of the method used in the instant specification to generate the hybrids employed in the method of the instant claims. For example, the Declarant presents an argument that Guo et al. employed Freund's complete adjuvant which cannot be administered more than once and which cannot be administered to humans. The Declarant further indicates that the method taught by Guo et al. requires the use of an "essential organ" (spleen)."

"It is the Examiner's position that adjuvants which could be administered more than once and which could be administered to humans were well-known in the art in the middle 1990's, as were sources of DCs besides the spleen. Regardless, note that no claims limiting the claimed method to humans are pending and only a few of the dependent claims limit the source of the DCs

to other than spleen. Also, regarding the "major advantages" of the method used in the instant specification to generate the hybrids employed in the method of the instant claims, it is noted that none of the advantages comprise claimed limitations. Accordingly, said advantages do not render the claimed method non-obvious."

"The Declarant argues that spleen cells are not a good source of DCs for the production of DC/tumor hybridomas."

"This seems a particularly curious argument given the fact that the hybridomas employed in the first six examples of the specification were produced using spleen cells, see page 32, *Example 2: Preparation of Murine Dendritic-Like Cells from the Spleen*. Also, note that this limitation, which the Declarant appears to be arguing is critical, is not recited in the independent claims."

"The Declarant makes an argument regarding the use of GM-CSF to induce DC-characteristics that is unclear to the Examiner. The Declarant appears to argue that the use of GM-CSF in the claimed method would not have been obvious."

"It is the Examiner's position that the use of GM-CSF in the culture of DC was well-known at the time of the invention and it is unclear to the Examiner why the Declarant appears to see some sort of non-obviousness in its use in the method of the instant claims."

"The Declarant argues "in the present invention it is suggested that said hybrids/hybridomas may be irradiated. However, said irradiation is not an essential step in the production of said vaccine."

"It is the Examiner's position that whether or not irradiation is essential, it is still obvious as it is unlikely that any patient would knowingly accept the administration of unattenuated or live tumor hybridomas."

"Applicant presents additional arguments. Applicant argues that, "it is only based on the present invention and by using impermissible hindsight that a skilled person may expect that by producing said hybrid/hybridomas, cells may be created having characteristics of both DC and tumor cells which are needed to induce an anti-tumor response in a subject"."

"In response to Applicant's argument that the examiner's conclusion of obviousness is based upon improper hindsight reasoning, it must be recognized that any judgment on obviousness is in a sense necessarily a reconstruction based upon hindsight reasoning. So long as it takes into account only knowledge which was within the level of ordinary skill at the time the claimed invention was made, and does not include knowledge gleaned only from the Applicant's disclosure, such a reconstruction is proper. See *In re McLaughlin*, 443 F.2d 1392, 170 USPQ 209 (CCPA 1971). It remains the Examiner's position that the combined references, in view of that which was known in the art at the time of the invention, render the instant methods obvious and not unpredictable, i.e., the hybrid of Guo et al. was functional, Sornasse et al. taught that DCs were better APCs than B cells, and it was known in the art that DC/tumor hybrids that maintained T cell activating capability could be produced."

Note that in this application, the claims now recite the limitation that the DCs be isolated from bone marrow, lymph or blood. These, however, are the most well-known and obvious sources of human DCs, indeed these are the most well-known and obvious sources of DCs from any patient that is expected to survive the donation. Also note that, regarding Applicant's (and Declarant's) assertions regarding the unpredictability of a DC tumor hybrid, the specification discloses at page 46, Example 9, that the methods of fusing DCs and tumors are merely an adaptation of a well-known method. There is no disclosure that said adaptation was anything other than routine or that the results were unexpected.

Applicant argues that the combined references do not teach the isolation of DCs from bone marrow, lymph or blood. Applicant argues that spleen is a disfavored source of DC and that the specification teaches away from the use of splenic DCs.

As set forth above, bone marrow, lymph or blood are the most obvious source of DCs from a patient. Note that the recitation of the term "patient", i.e., a subject being treated for a disease or condition, implies that it would be desirable to isolate the autologous DCs of the claimed invention in the least invasive and traumatic way possible. Accordingly, it would be obvious to the ordinarily skilled artisan, e.g., a physician, to isolate DCs from a patient's blood and not a

patient's spleen. Even in the situation wherein the donor is not the patient, sound scientific reasoning would dictate that the donor would prefer donating blood to donating a spleen. While this may not be Applicant's motivation for the isolation of DCs from sources other than spleen, it is never the less a motivation obvious to the ordinarily skilled artisan. Regarding the teaching away from the use of splenic DCs, the specification may teach that bone marrow, lymph, or blood derived DCs are more desirable for some uses, however, Examples 1-6 still teach the use of splenic DCs.

Applicant cites the second declaration of Inventor Moser, submitted in related application 09/951,848 and 09/802,397.

The Examiner's response to the Inventor's second declaration submitted in 09/802,397 (from the Office action of 4/25/05) is reiterated here.

"A review of the specification discloses that only hybrid clone 38 of Example 12 was tested for the ability to produce any relevant anti-tumor activity. The clone comprised a fusion employing a DC generated after 10 days in culture with GM-CSF and TNFα. The DCs after culture were MHC Class II+, B7.1+, and B7.2+. There is no disclosure as to whether or not the DCs after 10 days in culture were proliferating or not. Given this combined disclosure, it is more likely than not that the DCs employed in the example were unstable mature DCs, particularly given the expression of costimulatory molecules B7.1 and B7.2 that are more likely to be found on mature, non-proliferating DCs (see, for example, Morelli et al. (2001) which teaches that only mature DCs express B7.2 (CD86), and Shortman et al. (2002) which teaches that mature DCs are non-proliferating). Most certainly it has not been established that the DCs employed in the experiment were the proliferating DCs of the claims."

"As set forth in the second declaration of Inventor Moser, and the remarks of 2/07/05, the proliferating, less differentiated DCs of the claims are immature DCs. There is no evidence of record, however, that an immature DC (and, thus, a DC/tumor hybrid comprising an immature DC) would be capable of producing the required response. The prior art appears to teach the opposite. See, for example, Jonuleit et al. (2000) which teaches that stimulation of naïve T cells with immature DCs results in T cells that are irreversibly proliferation impaired

and produce IL-10 (see Results). Dhodapkar et al. extend these findings by showing that immature DCs *in vivo* lead to antigen-specific T cell inhibition (see Results, particularly Figure 2B). Again, the reference teaches that immature DCs would not likely produce an anti-tumor response. Even the Inventors' own work confirms the finding that immature DCs are not inducers of an immune response, see de Heusch et al. 2004 (Figure 3F)."

Applicant argues that, "Examples 1-6 of the present specification also demonstrate that DC/tumor cell hybrids could not be produced using spleen as the DC source.

It is unclear how Applicant can make this argument as splenic DCs were the source of the DCs used in the Examples and hybrids were produced. Whether or not spleen is the preferred source for DCs, it is still a source disclosed in the Examples of the specification. And regardless, as set forth above, blood is the most obvious source of DCs obtained from any donor expecting to survive the donation.

6. Claims 2, 12, 33, 42, 43, 44, 46, 47, 48, stand rejected under 35 U.S.C. § 103(a) as being unpatentable over Guo et al. (1994, IDS) in view of Sornasse et al. (1992), as applied to Claims 1, 5, 6, 7, 9, 10, 11, 16, 17, 18, 20, 21, 22, 26, 27, 28, and 29 above, and in further view of U.S. Patent No. 5,851,756.

As set forth previously, Guo et al. and Sornasse et al. have been discussed, supra. The references differ from the claimed invention in that they do not teach the induction of DC characteristics before using said hybrids/hybridomas, nor the induction of said characteristics using GM-CSF.

The '756 patent teaches the induction of DC characteristics using GM-CSF (see particularly Example I). The reference further teaches that DC exist in relatively small numbers in blood, thus the induction of DC (and thus, DC characteristics) in GM-CSF before use provides a method to increase the number of said DCs (see particularly column 4, line 63 - column 5, line 9).

It would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to produce the hybrids/hybridomas of Guo et al. and Sornasse et al., by the method of Guo et al., substituting a DC induced with GM-CSF before use, as taught by the '756 patent, for the B cell in said hybrids/hybridomas. One of ordinary skill in the art at the time of the invention would have been motivated to induce DC (and thus, DC characteristics) with GM-CSF before use because DC exist in relatively small numbers in blood, thus the induction of DC in GM-CSF before use provides a method to increase the number of said DCs, as taught by the '756 patent.

Applicant argues that as the rejections under Guo et al. and Sornasse et al. are deficient, this rejection is deficient.

See the Examiner's response above.

7. Claims 50-52, and 54-56 are rejected under 35 U.S.C. § 103(a) as being unpatentable over Guo et al. (1994, IDS) in view of Sornasse et al. (1992), as applied to Claims 1, 4, 5, 6, 7, 9, 10, 11, 15, 16, 17, 18, 20, 21, 22, 25, 26, 27, 28, and 29 above, and in further view of U.S. Patent No. 5,637,483.

As set forth previously, Guo et al. and Sornasse et al. have been discussed, supra. The references differ from the claimed invention in that they do not teach the treatment of the hybrids/hybridomas with irradiation before using to prevent proliferation.

The '483 patent teaches the treatment of a tumor cell-containing anti-tumor vaccine with irradiation before using to prevent proliferation (see particularly column 3, lines 65-67 and column 14, lines 3-4).

It would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to produce the hybrids/hybridomas of Guo et al. and Sornasse et al., by the method of Guo et al. and employ irradiation before using, as taught by the '483 patent. One of ordinary skill in the art at the time of the invention would have been motivated to treat the hybrids/hybridomas with irradiation before using to prevent proliferation, as taught by the '483 patent.

Applicant argues that as the rejections under Guo et al. and Sornasse et al. are deficient, this rejection is deficient.

See the Examiner's response above.

Applicant argues that as the rejections under Guo et al. and Sornasse et al. are deficient, this rejection is deficient.

See the Examiner's response above.

8. Claims 13, 14, 23, and 24 are rejected under 35 U.S.C. § 103(a) as being unpatentable over Guo et al. (1994, IDS) in view of Sornasse et al. (1992), as applied to Claims 1, 5, 6, 7, 9, 10, 11, 16, 17, 18, 20, 21, 22, 26, 27, 28, and 29 above, and in further view of Reid et al.

As set forth previously, Guo et al. and Sornasse et al. have been discussed, supra. The references differ from the claimed invention in that they do not teach the use of HAT for the killing of unfused drug-sensitive immortal tumor cells.

Reid et al. teaches the use of the HPRT gene to create a drug-sensitive cell for convenience of selection and killing employing multiple selectively toxic agents including HAT (see particularly page 4299, column 1).

It would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to produce the hybrids/hybridomas of Guo et al. and Sornasse et al., by the method of Guo et al. employing the HPRT gene of Reid et al. One of ordinary skill in the art at the time of the invention would have been motivated to employ the HPRT gene in the hybrids/hybridomas given the teachings of Reid et al. that the introduction of the HPRT gene creates a drug-sensitive cell for convenience of selection and killing employing multiple selectively toxic agents including HAT.

Applicant argues that as the rejections under Guo et al. and Sornasse et al. are deficient, this rejection is deficient.

See the Examiner's response above.

9. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

10. Claims 13, 14, 23, 24, 34, and 35 stand rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention, specifically:

A) The "said drug" in Claims 13, 23, and 34 has no antecedent basis in Claim 10, 21, and 31, respectively.

Applicant argues that "said drug" refers to the recitation of "drug-sensitive" within Claims 13, 23, and 35.

Applicant is advised that "drug-sensitive" within the claims refers to DCs or tumor cells and not drugs. Accordingly, the rejection is proper.

11. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

12. Claims 1, 2, 5-7, 9-14, 16-18, 20-24, 26-28, 30-35, 37-39, and 41-57 are rejected under 35 U.S.C. § 112, first paragraph, as the specification does not contain a written description of

the claimed invention, in that the disclosure does not reasonably convey to one skilled in the relevant art that the inventor(s) had possession of the claimed invention at the time the application was filed. This is a new matter rejection.

As set forth previously, The specification and the claims as originally filed do not provide support for the invention as now claimed, specifically, the recitation of:

A) The method of producing a fused cell product "for the reduction of the number of tumor cells in a patient", in Claims 1, 10, and 21.

B) The method of producing a fused cell product "using PEG", in Claims 9, 20, 30, and 41.

C) The method of producing a fused cell product comprising:
"(b) analyzing tumor-associated antigens of said tumor sample,
(c) providing an established cell line comprising immortal human tumor cells having at least one tumor-associated antigen in common with said tumor sample", in Claim 31.

Applicant's arguments, filed 6/13/05, have been fully considered but they are not persuasive. Applicant argues that regarding A), support can be found at pages 60 and 15 of the specification.

Applicant is advised that page 60 discloses only the protection of mice from the growth of P815 cells. Page 15 discloses only the "rejection of residual tumor as measured by its reduction in size and by the survival of the patient" and refers to experiments in mice (Example 5C and Example 12). None of these disclosures comprise the generic limitations of the claims.

Applicant argues that regarding B), support can be found in Examples 3, 9, and 12 of the specification and that the use of PEG to promote cell fusion was known in the art.

The Examples of the specification disclose only the fusion of P815 and 143B tumor cells and not the generic PEG fusion of the claims. Regarding that which is well known in the art, well known in the art is not the standard for the introduction of new matter, not disclosed in the specification or claims as filed, into the instant claims.

Applicant argues that regarding C), support can be found at pages 25 and 29-30 of the specification.

A review of the specification shows that none of the cites disclose the analyzing step (b) in conjunction with step (c) of the claim.

13. The following are new grounds of rejection necessitated by Applicant's amendment.

14. Claims 21-24, 26-31, 44, and 52 are rejected under 35 U.S.C. § 112, first paragraph, as the specification does not contain a written description of the claimed invention, in that the disclosure does not reasonably convey to one skilled in the relevant art that the inventor(s) had possession of the claimed invention at the time the application was filed. This is a new matter rejection.

The specification and the claims as originally filed do not provide support for the invention as now claimed, specifically, the recitation of:

A method for producing DC/tumor hybrids comprising …

(c) providing an immortal cell line comprising immortal autologous or HLA compatible or allogeneic DCs by isolation of DCs from bone marrows lymph or blood or preparing said DCs by differentiating in vitro proliferating DC precursors isolated from bone marrow, lymph or blood.

Applicant indicates that support for the new limitation can be found at pages 25, 28-30 or 60 of the specification.

A review of the specification reveals no support for the immortal cell line DCs of the claim being isolated from these sources.

15. No claim is allowed.

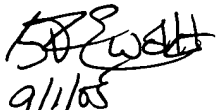
16. Applicant's IDS, submitted 5/25/05, has been lined through and has not been considered because it is unclear how Applicant's attorney can reasonably state that "no item of information in this statement" … "to my knowledge after making reasonable inquiry, was known to any individual designated in 37 C.F.R. j 1.56(c) more than three months prior to the filing of this Information Disclosure Statement", given that the de Heusch et al. reference is the work of Inventors Oberdan, Theilemans and Moser.

17. Applicant's amendment or action necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL.** See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 C.F.R. 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 C.F.R. 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

18. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Dr. Gerald Ewoldt whose telephone number is (571) 272-0843. The examiner can normally be reached Monday through Thursday from 7:30 am to 5:30 pm. A message may be left on the examiner's voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached on (571) 272-0841.

**Please Note**: Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).


9/1/05

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